

WHAT IS CLAIMED IS:

1. A method for generating a molecular profile of genomic DNA by hybridization of a genomic DNA target to an immobilized nucleic acid probe, comprising the following steps:

5 (a) providing a plurality of nucleic acid probes comprising a plurality of immobilized nucleic acid segments;

(b) providing a sample of target nucleic acid comprising fragments of genomic nucleic acid labeled with a detectable moiety, wherein each labeled fragment consists of a length smaller than about 200 bases; and

10 (c) contacting the genomic nucleic acid of step (b) with the immobilized probes of step (a) under conditions allowing hybridization of the target nucleic acid to the probe nucleic acid.

15 2. The method of claim 1, wherein each labeled fragment consists of a length no more than about 150 bases.

20 3. The method of claim 2, wherein each labeled fragment consists of a length no more than about 100 bases.

4. The method of claim 3, wherein each labeled fragment consists of a length no more than about 50 bases.

25 5. The method of claim 4, wherein each labeled fragment consists of a length no more than about 30 bases.

6. The method of claim 3, wherein each labeled fragment consists of a length between about 30 bases and about 150 bases.

30 7. The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure comprising random priming, nick translation, amplification, or equivalent, of a sample of genomic nucleic acid to generate segments of

target genomic nucleic acid; followed by a step comprising fragmentation or enzymatic digestion, or both, of the segments to generate a sample of target genomic nucleic acid consisting of sizes smaller than about 200 bases.

5 8. The method of claim 7, wherein the random priming, nick translation, amplification, or equivalent, of the sample of genomic nucleic acid to generate segments of target genomic nucleic acid incorporates detectably labeled base pairs into the segments.

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16 9. The method of claim 8, wherein the detectable label comprises Cy3™ or Cy5™ or equivalent.

17 10. The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure comprising fragmentation of a genomic DNA to sizes smaller than about 200 bases by DNase enzyme, or equivalent, digestion of the segments.

18 11. The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure comprising fragmentation of a genomic DNA to sizes smaller than about 200 bases by applying shearing forces sufficient to fragment genomic DNA followed by DNase enzyme, or equivalent, digestion of the sheared DNA.

19 12. The method of claim 1, wherein the conditions allowing hybridization of the target nucleic acid to the probe nucleic acid comprise stringent hybridization conditions.

20 25 13. The method of claim 12, wherein the stringent hybridization conditions comprise a temperature of about 60°C to about 65°C.

21 14. The method of claim 1, wherein the target nucleic acid consists essentially of DNA derived from a human.

15. The method of claim 1, wherein the sample of target genomic nucleic acid comprises sequences representing a defined part of or substantially an entire chromosome.

5 16. The method of claim 15, wherein the sample of target genomic nucleic acid comprises sequences representing substantially an entire genome.

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10 17. The method of claim 15 or 16, wherein the chromosomal or genome is derived from a human.

15 18. A composition comprising a sample of target nucleic acid comprising fragments of genomic nucleic acid labeled with at least one detectable moiety, wherein each labeled fragment has a length smaller than about 200 bases and the sample of labeled target genomic nucleic acid comprises sequences representing a defined part of or substantially a complete chromosome, or substantially a complete genome.

20 19. The composition of claim 18, wherein the target nucleic acid consists essentially of human DNA.

20 20. The composition of claim 18, wherein the chromosome or genome is mammalian DNA.

21. The method of claim 20, wherein the DNA is human DNA.

25 22. The composition of claim 18, wherein each labeled fragment consists of a length no more than about 100 bases.

23. The composition of claim 22, wherein each labeled fragment consists of a length no more than about 50 bases.

24. The composition of claim 23, wherein each labeled fragment consists of a length no more than about 50 bases.

5 25. The composition of claim 22, wherein each labeled fragment consists of a length between about 30 bases and about 100 bases.

10 26. The composition of claim 18, wherein the detectable label comprises Cy3TM or Cy5TM or equivalent.

15 27. A kit comprising a sample of target nucleic acid and printed matter, wherein the target nucleic acid comprises fragments of genomic nucleic acid labeled with a detectable moiety, wherein each labeled fragment consists of a length smaller than about 200 bases and the sample of labeled target genomic nucleic acid comprises sequences representing substantially an entire chromosome or genome; wherein the printed matter comprises instructions on hybridizing the sample of target nucleic acid to a nucleic acid array.

20 28. A method for hybridizing a sample of labeled nucleic acid targets to a plurality of nucleic acid probes, comprising the following steps:

(a) providing a sample of nucleic acid targets comprising fluorescent-labeled nucleic acid fragments and a plurality of nucleic acid probes, wherein the fluorescent label is sensitive to oxidation;

25 (b) contacting the nucleic acid target and nucleic acid probe of step (a) under conditions allowing hybridization of the sample with the probe, wherein the hybridization conditions comprise use of a hybridization solution comprising at least one antioxidant,

wherein the amount of antioxidant in the solution is sufficient to inhibit the oxidation of the fluorescent label under the hybridization conditions.

30 29. The method of claim 28, wherein the fluorescent label comprises Cy5TM or equivalent.

30. The method of claim 28, wherein the fluorescent dye comprises a rhodamine, a fluorescein or an aryl-substituted 4,4-difluoro-4a, 4a-diaza-s-indacene dye or equivalents.

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31. The method of claim 28, wherein the antioxidant is present in the hybridization solution at a concentration of about 25 mM to about 1000 mM.

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32. The method of claim 31, wherein the antioxidant is present in the hybridization solution at a concentration of about 50 mM to about 500 mM.

33. The method of claim 28, wherein the antioxidant comprises a mercapto-containing compound.

34. The method of claim 33, wherein the mercapto-containing compound comprises a 2-mercaptopethylamine, a thiol N-acetylcysteine, an ovothiol, a 4-mercaptopimidazole.

35. The method of claim 28, wherein the antioxidant comprises an antioxidant vitamin-containing compound.

36. The method of claim 35, wherein the antioxidant vitamin-containing compound comprises an ascorbic acid (Vitamin C) or a tocopherol (Vitamin E).

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37. The method of claim 28, wherein the antioxidant comprises a propyl gallate.

38. The method of claim 28, wherein the antioxidant comprises a beta-carotene.

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39. The method of claim 28, wherein the antioxidant comprises a butylated hydroxytoluene (BHT) or a butylated hydroxyanisole (BHA).

5 40. A composition comprising a sample of Cy5™-labeled nucleic acid or equivalent in a solution comprising at least one antioxidant.

10 41. The composition of claim 40, wherein the antioxidant is present in a hybridization solution at a concentration of about 25 mM to about 1000 mM.

15 42. The composition of claim 41, wherein the antioxidant is present in a hybridization solution at a concentration of about 50 mM to about 500 mM.

20 43. The composition of claim 40, wherein the antioxidant comprises a mercapto-containing compound.

25 44. The composition of claim 43, wherein the mercapto-containing compound comprises a 2-Mercaptoethylamine, a thiol N-acetylcysteine, an ovothiol, a 4-mercaptopimidazole.

30 45. The composition of claim 40, wherein the antioxidant comprises an antioxidant vitamin-containing compound.

46. The composition of claim 45, wherein the antioxidant vitamin-containing compound comprises ascorbic acid (Vitamin C) or a tocopherol (Vitamin E).

25 47. The method of claim 40, wherein the antioxidant comprises a propyl gallate.

30 48. The method of claim 40, wherein the antioxidant comprises a betacarotene.

49. The method of claim 40, wherein the antioxidant comprises a butylated hydroxytoluene (BHT) or a butylated hydroxyanisole (BHA).

5 50. A kit comprising a sample of fluorescent dye-labeled nucleic acid or equivalent in a solution comprising at least one antioxidant and printed matter, wherein the printed matter comprises instructions on using the fluorescent dye-labeled nucleic acid in a hybridization reaction with another nucleic acid.

10 51. The kit of claim 50 further comprising a hybridization complex wash solution comprising at least one antioxidant.

15 52. The kit of claim 50, wherein the fluorescent dye comprises a Cy5™ or equivalent.

20 53. The kit of claim 50, wherein the fluorescent dye comprises a rhodamine, a fluorescein or an aryl-substituted 4,4-difluoro-4-bora-3a, 4a-diaza-s-indacene dye or equivalents.

25 54. A method for hybridizing a sample of nucleic acid targets to a plurality of immobilized nucleic acid probes, comprising the following steps:

(a) providing a sample of nucleic acid targets and a plurality of immobilized nucleic acid probes;

(b) contacting the nucleic acid target and nucleic acid probe of step (a) under conditions allowing hybridization of the sample with the probe, wherein the hybridization conditions comprise a controlled hybridization environment comprising an unsaturated humidity environment.

30 55. The method of claim 54, wherein the unsaturated humidity environment is controlled at about 90% humidity, about 80% humidity, about 70% humidity, about 60% humidity, about 50% humidity, about 40% humidity, about 30% humidity, or about 20% humidity.

56. The method of claim 54, wherein the humidity of the controlled environment is periodically changed during the hybridization of step (b).

5 57. The method of claim 56, wherein the humidity is periodically changed at about three hour intervals, at about two hour intervals, at about one hour intervals, at about 30 minute intervals, at about 15 minute intervals or at about 5 minute intervals, or a combination thereof.

10 58. The method of claim 54, wherein the hybridization conditions comprise a controlled temperature environment.

15 59. The method of claim 58, wherein the temperature of the controlled environment is periodically changed during the hybridization of step (b).

20 60. The method of claim 59, wherein the temperature is periodically changed at about three hour intervals, at about two hour intervals, at about one hour intervals, at about 30 minute intervals, at about 15 minute intervals or at about 5 minute intervals, or a combination thereof.

25 61. A composition comprising an array of immobilized nucleic acids in a housing, wherein the housing comprises a component to measure and control the humidity in the housing.

62. The composition of claim 61, wherein the housing further comprises a component to measure and control the temperature in the housing.

63. The composition of claim 62, wherein the housing further comprises a component that allows programmable or preset control of the humidity and the temperature.

64. An array of immobilized probe nucleic acids in a humidity-controlled housing, wherein the housing comprises a means to control the amount of humidity in the housing during hybridization of the probes to a target in an aqueous hybridization solution.

5 65. An array of immobilized probe nucleic acids in a humidity-controlled housing, wherein the housing comprises a humidifier component that can control the amount of humidity in the housing during contact of the probes to an aqueous hybridization solution.

10 15 66. A kit comprising an array of immobilized nucleic acids in a housing and printed matter, wherein the housing comprises a component to control the amount of humidity in the housing, a component to control the temperature in the housing, and a component to preset or program control of the humidity and the temperature, and the printed matter comprises instructions for presetting or programming conditions in the housing to hybridize a target to the immobilized nucleic acids of the array under controlled hybridization conditions that comprise fluctuation of humidity and temperature during a nucleic acid hybridization step.

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